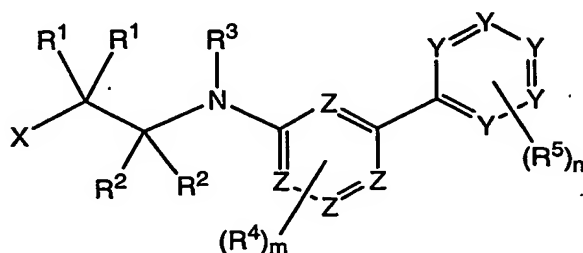


What is claimed is:

1. A compound for modulating kinase activity, particularly Tie-2, of Formula I,



I

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

X is selected from -H, -OR⁶, -S(O)₀₋₂R⁶, -N(R⁶)R⁷, -O-N(R⁶)R⁷, -N(R⁶)OR⁶, -N(R⁶)N(R⁶)R⁷, absent, oxo, thiono, and imino, with the proviso that when X is oxo, thiono, or imino, there is only one R¹;

R¹ and R², at each occurrence, are each independently selected from -H, halogen, -CN, -NH₂, -NO₂, -OR⁶, -N(R⁶)R⁷, -S(O)₀₋₂R⁷, -SO₂N(R⁶)R⁷, -CO₂R⁶, -C(O)N(R⁶)R⁷, -N(R⁶)SO₂R⁷, -N(R⁶)C(O)R⁷, -N(R⁶)CO₂R⁷, -C(O)R⁶, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, absent, and optionally substituted lower heterocyclalkyl;

optionally two of R² together are oxo;

optionally, at least one pair of substituents, selected from two of R¹, two of R², and one each of R¹ and R², together with the corresponding carbon or carbons to which they are attached, form a first ring comprising between three and seven annular atoms, said first ring optionally substituted with between zero and four additional of R¹, each independently selected as defined above and optionally, when paired, together with the corresponding atom or atoms of the first ring to which they are attached, form a second ring comprising between three and seven annular atoms, said second ring optionally substituted with between zero and three of R¹;

R³ is selected from -H, optionally substituted lower alkyl, optionally substituted lower arylalkyl, optionally substituted aryl, optionally substituted heterocyclyl, and optionally substituted alkoxy;

optionally R³ and one of R², together with the atoms to which each is attached, form a third ring comprising between three and seven annular atoms, said third ring optionally

substituted with between zero and four additional of R^1 , each independently selected as defined above and optionally, when paired, together with the corresponding atom or atoms of the third ring to which they are attached, form a fourth ring comprising between three and seven annular atoms, said fourth ring optionally substituted with between zero and three of R^1 ;

optionally R^3 and one of R^1 , together with the atoms to which they are attached and the carbon to which R^2 is attached, form a fifth ring comprising between three and seven annular atoms, said fifth ring optionally substituted with between zero and four additional of R^1 , each independently selected as defined above and optionally, when paired, together with the corresponding atom or atoms of the fifth ring to which they are attached, form a sixth ring comprising between three and seven annular atoms, said sixth ring optionally substituted with between zero and three of R^1 ;

m is zero to four;

each of R^4 is independently selected from -H, halogen, -CN, -NH₂, -NO₂, -OR⁶, -N(R⁶)R⁷, -S(O)₀₋₂R⁷, -SO₂N(R⁶)R⁷, -CO₂R⁶, -C(O)N(R⁶)R⁷, -N(R⁶)SO₂R⁷, -N(R⁶)C(O)R⁷, -N(R⁶)CO₂R⁷, -C(O)R⁶, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl;

optionally two adjacent of R^4 , together with the two carbons to which they are attached, form a seventh ring fused with the aromatic ring system containing Z as in Formula I, said seventh ring comprising between five and seven atoms and substituted with zero to three additional of R^4 , provided said seventh ring together with the aromatic ring system containing Z as in Formula I does not constitute a 7-deazapurine;

each Y is independently either =C(R⁵)- or =N-, provided that there are no more than three of =N- in the aromatic ring bearing Y;

each Z is independently either =C(R⁴)- or =N-;

n is zero to five;

each R^5 is independently selected from -H, halogen, -CN, -NH₂, -NO₂, -OR⁶, -NR⁶R⁷, -S(O)₀₋₂R⁷, -SO₂NR⁶R⁷, -CO₂R⁶, -C(O)NR⁶R⁷, -N(R⁶)SO₂R⁷, -N(R⁶)C(O)R⁷, -N(R⁶)CO₂R⁷, -C(O)R⁶, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl; and

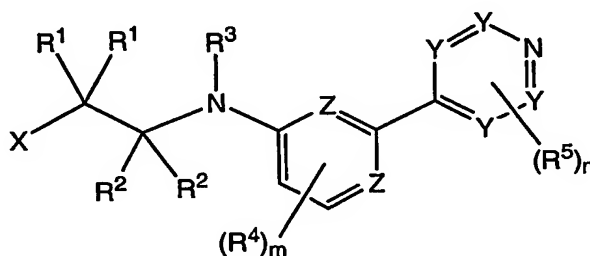
optionally two adjacent of R^5 , together with the two carbons to which they are attached, form an eighth ring fused with the aromatic ring system containing Y as in Formula I, said eighth ring comprising between five and seven atoms and substituted with zero to three additional of R^5 ;

R^6 is -H or R^7 ;

R^7 is selected from optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl; and

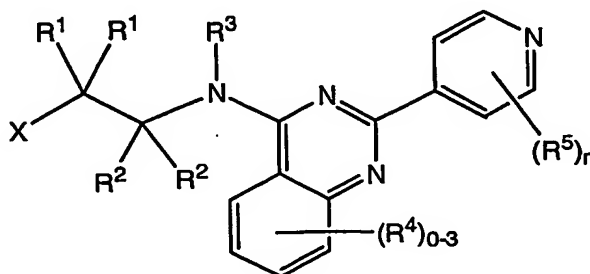
R^6 and R^7 , when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P.

2. The compound according to claim 1, of Formula II.



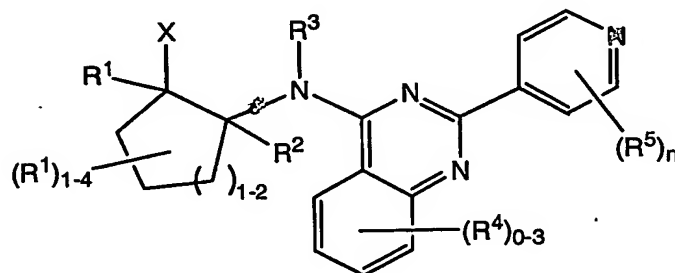
II

3. The compound according to claim 2, wherein at least one of Z is =N-.
4. The compound according to claim 2, wherein Z is =N-.
5. The compound according to claim 4, wherein Y is =C(R⁵)-.
6. The compound according to claim 5, of Formula III.



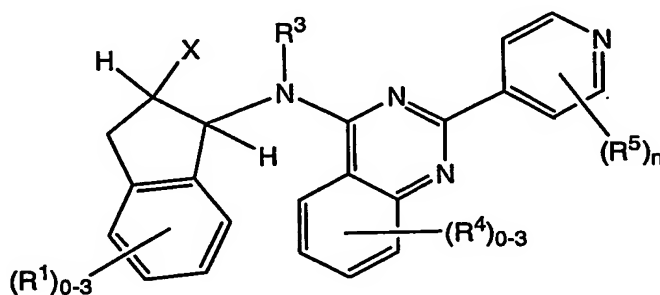
III

7. The compound according to claim 6, wherein one each of R^1 and R^2 , together with the corresponding carbons to which they are attached, form said first ring, said first ring comprising a saturated ring, said saturated ring optionally substituted with between zero and four additional of R^1 .
8. The compound according to claim 7, wherein said saturated ring is carbocyclic.
9. The compound according to claim 8, of Formula IV.



IV

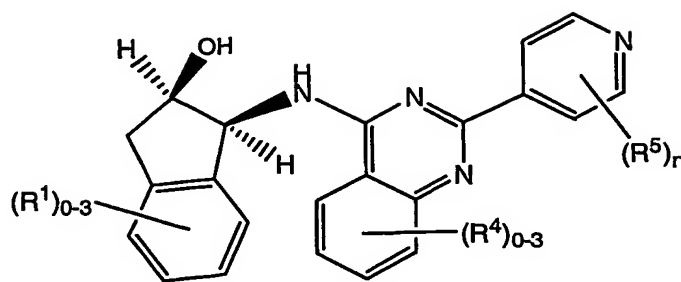
10. The compound according to claim 9, wherein X is selected from $-OR^6$, $-SR^6$, and $-N(R^6)R^7$.
11. The compound according to claim 10, wherein two of R^1 , together with the carbon or carbons to which they are attached, form said second ring.
12. The compound according to claim 11, wherein said second ring is a six-membered aryl, fused with said first ring, said second ring optionally substituted with between zero and three of R^1 .
13. The compound according to claim 12, of formula V.



V

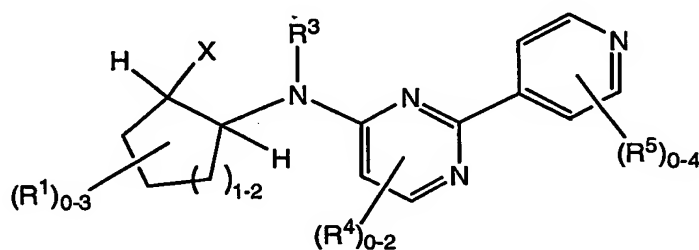
14. The compound according to claim 13, wherein X is $-OR^6$.
15. The compound according to claim 14, wherein R^3 is $-H$.
16. The compound according to claim 15, wherein X is $-OH$.

17. The compound according to claim 16, of formula VI.



VI

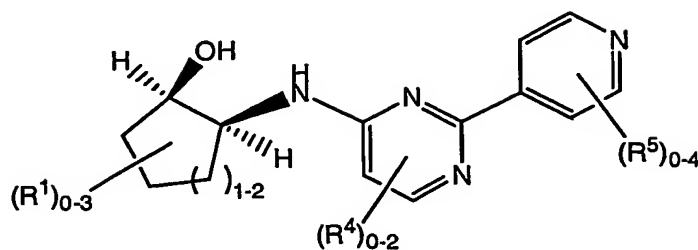
18. The compound according to claim 17, wherein R^1 , R^4 , and R^5 are -H.
19. The compound according to claim 5, of formula VII,



VII

20. The compound according to claim 19, wherein X is selected from $-OR^6$, $-SR^6$, and $-N(R^6)R^7$.
21. The compound according to claim 20, wherein X is -OH.
22. The compound according to claim 21, wherein R^3 is -H.
23. The compound according to claim 22, wherein at least one of R^1 is an optionally substituted aryl.
24. The compound according to claim 22, wherein at least one of R^4 is an optionally substituted aryl.
25. The compound according to claim 22, wherein at least one of R^1 is an optionally substituted phenyl.
26. The compound according to claim 22, wherein at least one of R^4 is an optionally substituted phenyl.

27. The compound according to claim 22, of formula VIII.



VIII

28. The compound according to claim 27, wherein two of R^4 , together with the aromatic annular atoms to which they are attached, form said seventh ring, said seventh ring comprising between zero and two nitrogens.

29. The compound according to claim 28, wherein said seventh ring is substituted with between zero and three additional of R^4 .

30. The compound according to claim 1, selected from Table 3.

Table 3

#	Name	Structure
1	N-cyclohexyl-2-pyridin-4-ylquinazolin-4-amine	
2	2-pyridin-4-yl-N-(2-pyrrolidin-1-ylethyl)quinazolin-4-amine	
3	N-cyclopentyl-2-pyridin-4-ylquinazolin-4-amine	
4	N-(cyclohexylmethyl)-2-pyridin-4-ylquinazolin-4-amine	

Table 3

#	Name	Structure
5	2-[(2-pyridin-4-ylquinazolin-4-yl)amino]ethanol	
6	3-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-1-ol	
7	N-[(4-fluorophenyl)methyl]-2-pyridin-4-ylquinazolin-4-amine	
8	N,N-dimethyl-N'-(2-pyridin-4-ylquinazolin-4-yl)ethane-1,2-diamine	
9	N-(2,3-dihydro-1H-inden-1-yl)-2-pyridin-4-ylquinazolin-4-amine	
10	N-(2-morpholin-4-ylethyl)-2-pyridin-4-ylquinazolin-4-amine	
11	4-[4-(2-pyridin-4-ylquinazolin-4-yl)piperazin-1-yl]phenol	

Table 3

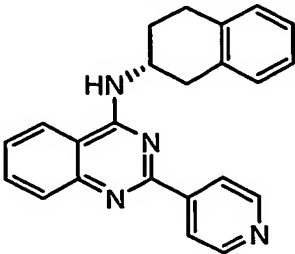
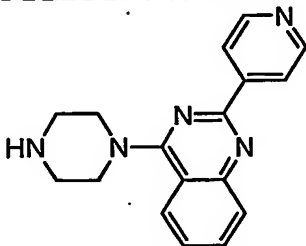
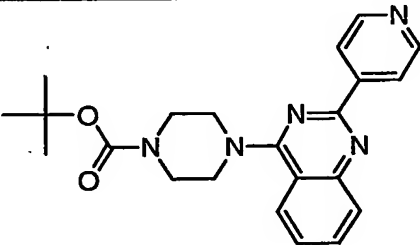
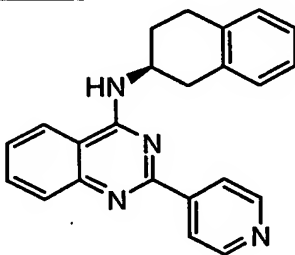
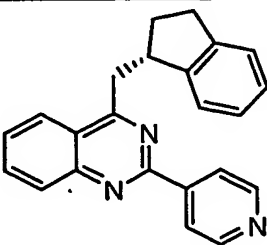
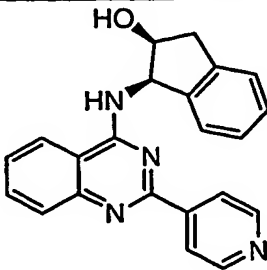
#	Name	Structure
12	2-pyridin-4-yl-N-[(2R)-1,2,3,4-tetrahydronaphthalen-2-yl]quinazolin-4-amine	
13	4-piperazin-1-yl-2-pyridin-4-ylquinazoline	
14	1,1-dimethylethyl 4-(2-pyridin-4-ylquinazolin-4-yl)piperazine-1-carboxylate	
15	2-pyridin-4-yl-N-[(2S)-1,2,3,4-tetrahydronaphthalen-2-yl]quinazolin-4-amine	
16	4-[(1S)-2,3-dihydro-1H-inden-1-ylmethyl]-2-pyridin-4-ylquinazoline	
17	(1R,2S)-1-[(2-pyridin-4-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	

Table 3

#	Name	Structure
18	(1S,2R)-1-[(2-pyridin-4-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
19	1,1-dimethylethyl 4-[(2-pyridin-4-ylquinazolin-4-yl)amino]piperidine-1-carboxylate	
20	2-pyridin-4-yl-N-[[2,4,6-tris(methoxy)phenyl]methyl]quinazolin-4-amine	
21	N-piperidin-4-yl-2-pyridin-4-ylquinazolin-4-amine	
22	N-[(1S,2S)-2-[(phenylmethyl)oxy]cyclopentyl]-2-pyridin-4-ylquinazolin-4-amine	
23	N-phenyl-N'-(2-pyridin-4-ylquinazolin-4-yl)benzene-1,4-diamine	

Table 3

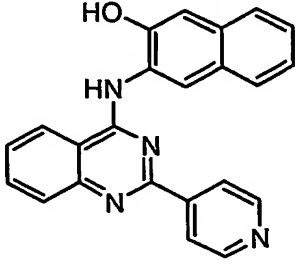
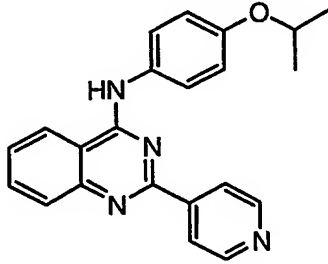
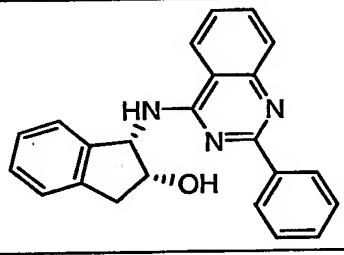
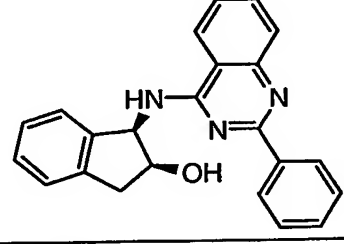
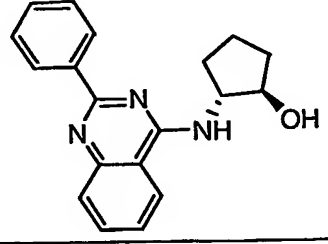
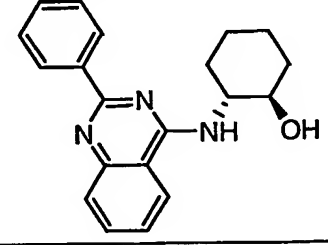
#	Name	Structure
24	3-[(2-pyridin-4-ylquinazolin-4-yl)amino]naphthalen-2-ol	
25	N-{4-[(1-methylethyl)oxy]phenyl}-2-pyridin-4-ylquinazolin-4-amine	
26	(1S,2R)-1-[(2-phenylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
27	(1R,2S)-1-[(2-phenylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
28	(1R,2R)-2-[(2-phenylquinazolin-4-yl)amino]cyclopentanol	
29	(1R,2R)-2-[(2-phenylquinazolin-4-yl)amino]cyclohexanol	

Table 3

#	Name	Structure
30	(1S,2R,3R,5R)-3-(hydroxymethyl)-5-[(2-phenylquinazolin-4-yl)amino]cyclopentane-1,2-diol	
31	(1S,2R)-1-[(6-chloro-2-pyridin-4-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
32	N-(2-piperazin-1-ylethyl)-2-pyridin-4-ylquinazolin-4-amine	
33	(1S,2R)-1-[(2-pyridin-3-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
34	(1R,2S)-1-[(2-pyridin-3-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
35	(1R,2R)-2-[(2-pyridin-3-ylquinazolin-4-yl)amino]cyclopentanol	

Table 3

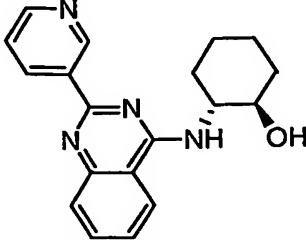
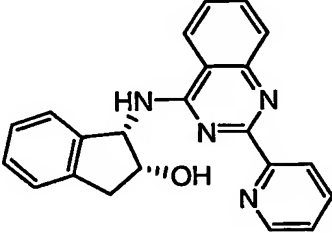
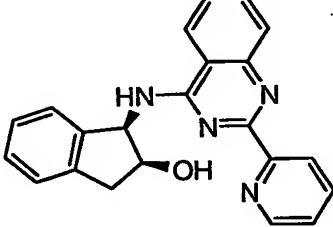
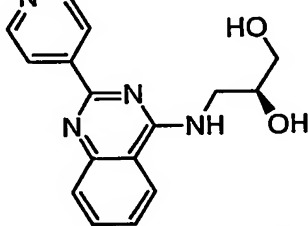
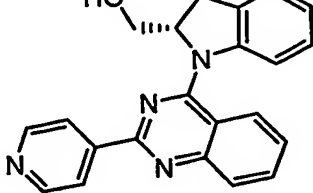
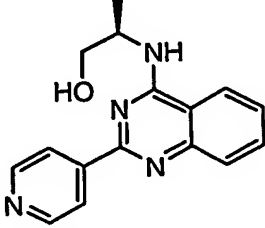
#	Name	Structure
36	(1R,2R)-2-[(2-pyridin-3-ylquinazolin-4-yl)amino]cyclohexanol	
37	(1S,2R)-1-[(2-pyridin-2-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
38	(1R,2S)-1-[(2-pyridin-2-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
39	(2S)-3-[(2-pyridin-4-ylquinazolin-4-yl)amino]propane-1,2-diol	
40	[(2S)-1-(2-pyridin-4-ylquinazolin-4-yl)-2,3-dihydro-1H-indol-2-yl]methanol	
41	(2R)-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-1-ol	

Table 3

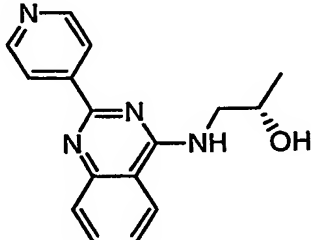
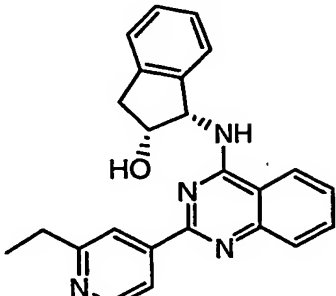
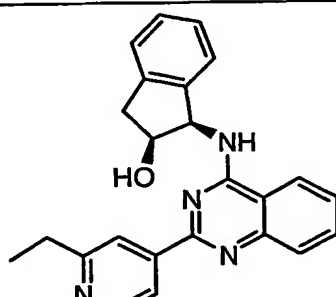
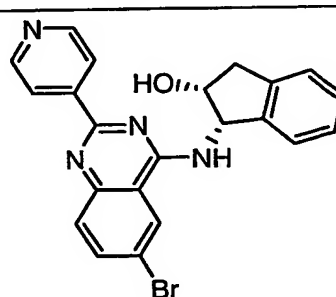
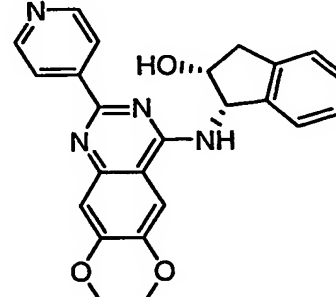
#	Name	Structure
42	(2S)-1-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-2-ol	
43	(1S,2R)-1-{[2-(2-ethylpyridin-4-yl)quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	
44	(1R,2S)-1-{[2-(2-ethylpyridin-4-yl)quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	
45	(1S,2R)-1-[(6-bromo-2-pyridin-4-yl)quinazolin-4-yl]amino]-2,3-dihydro-1H-inden-2-ol	
46	(1S,2R)-1-{[6,7-bis(methoxy)-2-pyridin-4-yl]quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	

Table 3

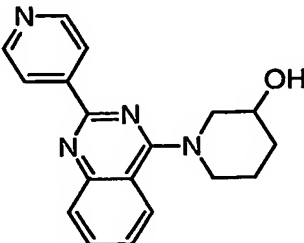
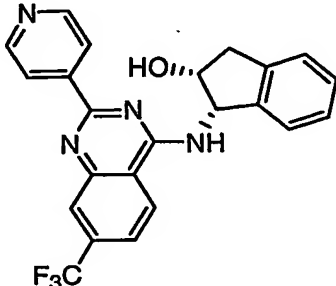
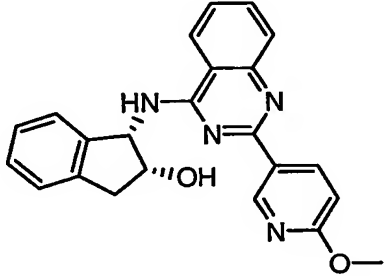
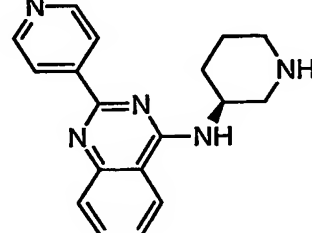
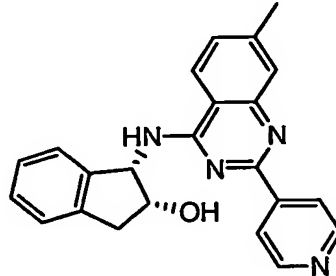
#	Name	Structure
47	1-(2-pyridin-4-ylquinazolin-4-yl)piperidin-3-ol	
48	(1S,2R)-1-([2-pyridin-4-yl-7-(trifluoromethyl)quinazolin-4-yl]amino)-2,3-dihydro-1H-inden-2-ol	
49	(1S,2R)-1-([2-[6-(methyloxy)pyridin-3-yl]quinazolin-4-yl]amino)-2,3-dihydro-1H-inden-2-ol	
50	N-[(3S)-piperidin-3-yl]-2-pyridin-4-ylquinazolin-4-amine	
51	(1S,2R)-1-[(7-methyl-2-pyridin-4-yl)quinazolin-4-yl]amino]-2,3-dihydro-1H-inden-2-ol	

Table 3

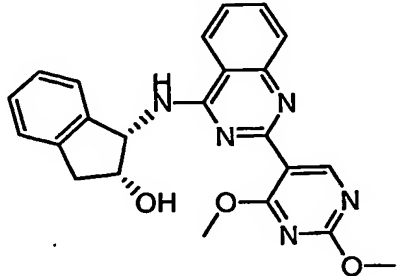
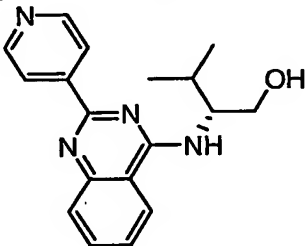
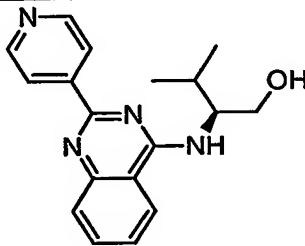
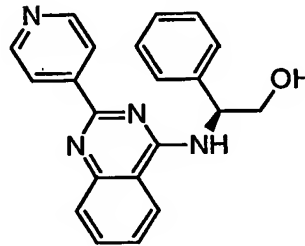
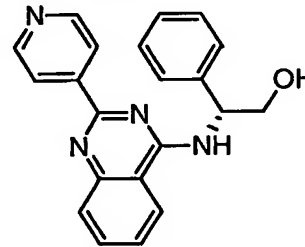
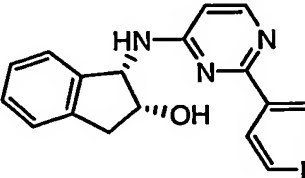
#	Name	Structure
52	(1S,2R)-1-((2-[2,4-bis(methyloxy)pyrimidin-5-yl]quinazolin-4-yl)amino)-2,3-dihydro-1H-inden-2-ol	
53	(2R)-3-methyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]butan-1-ol	
54	(2S)-3-methyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]butan-1-ol	
55	(2S)-2-phenyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]ethanol	
56	(2R)-2-phenyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]ethanol	
57	(1S,2R)-1-[(2-pyridin-4-ylpyrimidin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	

Table 3

#	Name	Structure
58	(1S,2R)-1-[(2-pyrazin-2-ylquinazolin-4-yl)amino]-2,3-dihydro-1H-inden-2-ol	
59	(1S,2R)-1-{[2-(4-aminopyridin-3-yl)quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	
60	(2R)-3-phenyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-1-ol	
61	(2S)-3-phenyl-2-[(2-pyridin-4-ylquinazolin-4-yl)amino]propan-1-ol	
62	2-[(phenylmethyl)(2-pyridin-4-ylquinazolin-4-yl)amino]ethanol	
63	(1S,2R)-1-{[2-(2-aminopyrimidin-4-yl)quinazolin-4-yl]amino}-2,3-dihydro-1H-inden-2-ol	

Table 3

#	Name	Structure
64	5-(4-([(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino)quinazolin-2-yl)pyridin-2-ol	
65	(1S,2R)-1-((2-[2-(methylthio)pyrimidin-4-yl]quinazolin-4-yl)amino)-2,3-dihydro-1H-inden-2-ol	
66	2-{4-[(2-pyridin-4-ylquinazolin-4-yl)amino]piperazin-1-yl}ethanol	
67	N-piperidin-1-yl-2-pyridin-4-ylquinazolin-4-amine	

31. A pharmaceutical composition comprising the compound according to any one of claims 1 - 30 and a pharmaceutically acceptable carrier.

32. A metabolite of the compound or the pharmaceutical composition according to any one of claims 1 -31.

33. A method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of a composition comprising at least one of the compound according to any of claims 1 - 30 and the pharmaceutical composition according to claim 31.

34. The method according to claim 33, wherein the kinase is Tie-2.
35. The method according to claim 34, wherein modulating the *in vivo* activity of Tie-2 comprises inhibition of Tie-2.
36. A method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of a composition comprising at least one of the compound according to any of claims 1 - 30 and the pharmaceutical composition according to claim 31.
37. A method of screening for a modulator of a Tie-2 kinase, the method comprising combining either a composition comprising at least one of the compound according to any of claims 1 -30 and the pharmaceutical composition according to claim 31, and at least one candidate agent and determining the effect of the candidate agent on the activity of said kinase.
38. A method of inhibiting proliferative activity in a cell, the method comprising administering an effective amount of at least one of the compound according to any of claims 1 - 30 and the pharmaceutical composition according to claim 31, to said cell.